PATENT COOPERATION TREATY

PCT

RECD 27 JUL 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 19026-1PC	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/11179	International filing date *(day/month/year)* 19 MAY 1999	Priority date *(day/month/year)* 20 MAY 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant TEIJIN LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17 NOVEMBER 1999	05 JULY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer RODNEY P. SWARTZ, PH.D. Telephone No. (703)308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/11179

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-40 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 41-45 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-9 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [X] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/11179

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-33	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-33	NO
Industrial Applicability (IA)	Claims	1-33	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-33 lack an inventive step under PCT Article 33(3) as being obvious over Queen et al in view of Morooka et al, and Hii, Schmitt et al, Downes et al, and Perera et al.
The claims are drawn to humanized antibodies which bind to VT2 and/or VT2 variant and neutralize the toxin.

Queen et al teach methods for producing humanized antibodies which are substantially non-immunogenic in humans, but retain substantially the same affinity as the donor (e.g., mouse) immunoglobulin to the antigen (Abstract; Col. 10, line 55 to col.68, line 27). Queen et al do not teach humanized antibody that binds specifically to VT2 or VT2v.

Morooka et al teach antibodies which bind to VT2 and VT2c and the use of the antibodies for treatment of patients suffering from hemolytic uremic syndrome (see entire reference).

HII teaches antibodies which bind to VT2, VT2v and the B subunit of VT2 (page 2705, section **Antisera**) which neutralize the toxins (page 2707, section **Neutralization studies**).

Schmitt et al teach monoclonal and polyclonal antibodies which bind to VT2 and neutralize the toxin (pages 1065-1067).

Downes et al teach monoclonal and polyclonal antibodies which bind to VT2 and neutralize the toxin (pages 1928-1930).

Perera et al teach monoclonal and polyclonal antibodies which bind to verotoxins and neutralize the toxin (pages 2127-2129).

It would have been obvious to humanize the antibodies taught by Morooka et al, and Hii, Schmitt et al, Downes et al, and Perera et al using the techniques of Queen et al in order to produce substantially nonimmunogenic antibodies for clinical treatment of patients suffering from hemolytic uremic syndrome.

---------- NEW CITATIONS ----------
(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): A61K 39/02, 39/40, 39/108, 39/395; C12N 5/00, 5/02, 5/06; C12P 21/04 and US Cl.: 424/133.1, 150.1, 236.1, 241.1; 435/70.21, 71.3, 328, 388.1, 388.4

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:
NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
MOROOKA et al. Anti-verocytotoxin (VT)1, VT2 and VT2c antibodies in commercial intravenous immune globulins in Japan. Acta Paediatrica Japonica. 1996, Vol. 38, pages 294-295, entire document.